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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------------------|-----------------------------|
| 10/584,811 | 07/10/2007 | Jean-Guy Lehoux | 2003390-0032 (ROBIC 01236 | 4922 |
| 24280 7590 06/09/2010 CHOATE, HALL & STEWART LLP TWO INTERNATIONAL PLACE BOSTON, MA 02110 | | | EXAMINER BLAND, LAYLA D | |
| | | | ART UNIT 1623 | PAPER NUMBER |
| | | | NOTIFICATION DATE 06/09/2010 | DELIVERY MODE ELECTRONIC |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

lbradley@choate.com
patentdocket@choate.com
jhess@choate.com

| | | | | |
|------------------------------|------------------------|--|---------------------|--|
| Office Action Summary | Application No. | | Applicant(s) | |
| | 10/584,811 | | LEHOUX ET AL. | |
| | Examiner | | Art Unit | |
| | LAYLA BLAND | | 1623 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 April 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 13-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____. | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Applicant's election without traverse of Group II, claims 1-12, in the reply filed on April 30, 2010 is acknowledged. Claims 1-19 are pending. Claims 13-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 30, 2010. Claims 1-12 are examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 10 recites "molecular weight of about between 7 kDa and several hundreds kDa." The upper limit of this range is unclear, because "several" could mean 2, or 3, or more. One web definition of "several" is "of an indefinite number more than 2 or 3 but not many." The specification does not provide a definition for "several" or guidance for determining the intended upper limit of molecular weight. Thus, the skilled artisan could not ascertain the upper limit of molecular weight required by claim 10.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 and 9-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Berthold et al. (Journal of Controlled Release 39 (1996) 17-25).

Berthold teaches a method wherein chitosan of molecular weight 70,000, 750,000 and 2,000,000 and a deacetylation grade of about 87% was dissolved in an aqueous solution of 2% acetic acid (pH roughly estimated at about 2.5). A solution of sodium sulfate was added dropwise to form microspheres which were purified by centrifugation and washing with water [page 18, Reagents and chemicals and Preparation of chitosan microspheres]. The microspheres are used as a drug carrier [see abstract], so it is considered that sodium sulfate is suitable for biomedical applications. Although Berthold is silent with respect to the yield of precipitated chitosan, claim scope is not limited by claim language that does not require steps to be performed or does not limit a claim to a particular structure, and a “whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.” See MPEP 2106 and 2111.04. Claim 9 is interpreted as simply expressing the intended result of the process of claim 1 and does not limit claim scope.

Claims 1-4, 6, and 9-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Struszczyk et al. (WO 03/066682 A1, August 14, 2003, PTO-1449 submitted December 5, 2007).

Struszczyk teaches a process wherein chitosan (MW 796 kD and DD 85.6%) was mixed with a 2% aqueous solution of acetic acid (pH about 2.5). Sodium carbonate was added and chitosan precipitated in microcrystalline form. The dispersion was concentrated by centrifugation and washed with water [page 6, Example VI]. The product is acceptable for medical and pharmaceutical uses, so sodium carbonate is considered suitable for biomedical applications. Although Struszczyk is silent with respect to the yield of precipitated chitosan, claim scope is not limited by claim language that does not require steps to be performed or does not limit a claim to a particular structure, and a “whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.” See MPEP 2106 and 2111.04. Claim 9 is interpreted as simply expressing the intended result of the process of claim 1 and does not limit claim scope.

Claims 1-7 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Anderson et al. (GB 2385050 A, August 13, 2003).

Anderson teaches a method wherein an aqueous solution of chitosan hydrochloride (MW 200 kD and DD 84%) at pH 4.2 was treated with sodium citrate and precipitation occurred. Precipitation was also done using pentasodium tripolyphosphate. [page 14, Examples 1 and 2]. Analysis of the water after precipitation

with sodium citrate showed that no chitosan could be found in the water [page 16, second paragraph], so at least 90% of the chitosan in solution was precipitated. In another example, chitosan hydrochloride was dissolved in tap water and the pH adjusted to 4-5 by addition of hydrochloric acid. Sodium citrate was added and precipitation occurred, leaving no detectable amounts of chitosan in the water [pages 16-17, Example 6]. In another example, chitosan was precipitated using sodium citrate and sodium alginate [page 21, Example 12].

Claims 1-4, 6-9, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Sannan et al. (US 4,267,313, May 12, 1981).

Sannan teaches a method wherein chitosan is dissolved in aqueous acetic acid (pH about 2.5) and sodium isocyanate (chaotropic salt) and sodium carbonate (kosmotropic salt, and food-compatible) were added to form a precipitate. The precipitate was separated by filtration and washed with water. [column 6, Example 4]. Chitosans having degree of deacetylation preferably about 80% and viscosity in the range of 10-2,000 cps are suitable [column 1, lines 57-64]. Although Sannan is silent with respect to the yield of precipitated chitosan, claim scope is not limited by claim language that does not require steps to be performed or does not limit a claim to a particular structure, and a “whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.” See MPEP 2106 and 2111.04. Claim 9 is interpreted as simply expressing the intended result of the process of claim 1 and does not limit claim scope.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sannan et al. (US 4,267,313, May 12, 1981) in view of Berthold et al. (Journal of Controlled Release 39 (1996) 17-25).

Sannan teaches as set forth above, but teaches filtration of chitosan instead of centrifugation, and is silent with respect to the molecular weight of chitosan used in the examples. Although Sannan teaches filtration to remove precipitated chitosan from solution, centrifugation has been used for removing precipitated chitosan from solution, as taught by Berthold. The skilled artisan would use either filtration or centrifugation

because they are both effective for removing precipitated chitosan from solution.

Sannan teaches that the molecular weight of chitosan is not critical, so the skilled artisan would expect that any molecular weight could be used. As taught by Berthold, chitosans of molecular weight 70,000, 750,000 and 2,000,000 have been successfully salted out, so the skilled artisan would expect that any of those could be used in Sannan's method.

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mallon et al. (US 5,733,462, March 31, 2998) in view of Singla et al. (Journal of Pharmacy and Pharmacology 2001, 53:1047-1067) and Berthold et al. (Journal of Controlled Release 39 (1996) 17-25).

Mallon teaches methods for precipitating cationic polymers using salt solutions [see abstract]. The process comprises mixing, in any order, water, at least one cationic water-soluble polymer, an effective amount of kosmotropic salt, and an effective amount of chaotropic salt to form an aqueous composition comprising at least one precipitated cationic water-soluble polymer [column 5, lines 14-32]. Water-soluble cationic polymers are precipitated more effectively by a combination of chaotropic and kosmotropic salts than by either salt alone [column 8, lines 27-42]. Exemplified salt combinations include ammonium sulfate and sodium thiocyanate or sodium sulfate and sodium thiocyanate [Figures 1 and 2].

Mallon teaches precipitation of cationic polymers, but does not teach precipitation of chitosan in particular.

Singla teaches that chitosan is a cationic polymer which is soluble at acidic pH [page 1049, Table 3]. A high electrolyte concentration results in a salting-out effect leading to precipitation of chitosan from the solution [page 1049, first full paragraph].

Berthold teaches as set forth above, that chitosan can be precipitated from solution using sodium sulfate.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to carry out the precipitation or salting-out of chitosan using a combination of kosmotropic and chaotropic salt. Mallon teaches that precipitation of cationic polymers is more effective using a kosmotropic and a chaotropic salt than either alone. Chitosan is a cationic polymer which is precipitated or salted-out from solution using salts such as sodium sulfate. The skilled artisan would precipitate chitosan using a combination of salts because Mallon teaches that a combination is more effective than a single salt. Mallon's examples include ammonium sulfate and sodium thiocyanate or sodium sulfate and sodium thiocyanate and precipitation of chitosan using sodium sulfate alone is known, as taught by Berthold. The skilled artisan would expect that the combination of ammonium sulfate and sodium thiocyanate or sodium sulfate and sodium thiocyanate would effectively precipitate chitosan because sodium sulfate is already known for that purpose and Mallon teaches that addition of another salt such as sodium thiocyanate would give a more effective precipitation.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Layla Bland/
Examiner, Art Unit 1623